241

CD34+ STEM CELL SELECTION AND CD3+ ADDBACK FOR PEDIATRIC PATIENTS RECEIVING MATCHED UNRELATED ADULT DONOR (MUD) PERIPHERAL BLOOD STEM CELL TRANSPLANTATION (PBSCT) IS ASSOCIATED WITH RAPID MYELOID ENGRAFTMENT AND LOW RISK OF BOTH POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER (PTLD) AND GRADE 2-4 ACUTE GRAFT VERSUS HOST DISEASE (AGVHD)

Geyer, M.B.[1], Jacobson, J.S.[2], Fearon, N.[1], Satwani, P.[1], Bhatia, M.[1], George, D.[1], Bradley, M.B.[1], Garvin, J.H.[1], Harrison, L.[1], Morris, E.[1], Fanelli, C.[1], Semidei-Pomales, M.[3], Daniel-Johnson, J.A.[3], Schwartz, J.[3], Baxter-Lowe, L.A.[4], Cairo, M.S.[1,3,5] [1]Morgan Stanley Children's Hospital, New York-Presbyterian Hospital, Columbia University, NY; [2]Columbia University, New York, NY; [3]Columbia University, New York, NY; [4]University of California, San Francisco, CA; [5]Columbia University, New York, NY

Background: Positive selection of CD34 stem cells is a method of depletion of T cells responsible for severe aGVHD (Lang et al., Blood, 2003). CD34-selected haploidentical SCT in children with leukemia and nonmalignant diseases is associated with sustained engraftment and low risk of aGVHD (Lang/Handgretinger, BMT, 2008). Myeloablative conditioning (MAC) followed by CD34-selected MUD PBSCT with a CD3 dose of 5×10^5/kg carries high risk of chronic GVHD (Bunin et al., BMT, 2006). We sought to determine engraftment, survival, immune reconstitution (IR) and frequency of PTLD and GVHD in pediatric patients at risk of severe aGVHD following CD34-selected MUD PBSCT.

Methods: The Isolex 300i (Nexell, Irvine, CA) immunomagnetic cell selection system was used for CD34 selection with a goal of achieving ≥ 5 x10^6 CD34/kg PBSC. T cells were added back to reach a total CD3 dose of 1.0-2.6$\times10^5$/kg. Conditioning was MAC in 57% vs. reduced intensity (RIC) in 43%. GVHD prophylaxis consisted only of tacrolimus. Supportive care was as we have previously described (Bradley/Cairo, BMT, 2007).

Results: Fourteen pts, median f/u of 451 d, median age of 15.0 yrs (10-23); 1:1 M:F, HLA match 29% 10/10, 36% 9/10, 26% 8/10, 64% malignant (56/44% poor/average risk). Cell selection resulted in median CD34 recovery of 59% and 4.33 CD3 log depletion (Table 1).

All 14 pts engrafted neutrophils (median day 14, range 9-27). Of 12 evaluable pts, 10 (83%) engrafted platelets (median day 32, range 21-44). No pts developed PTLD. One pt (7%) developed CMV infection. Probabilities of grade II-IV aGVHD and chronic GVHD were 14.3% (95% CI 0-31%) and 36.4% (1-59%) respectively. Day 100 mortality was 7%. The probability of 1-year OS was 84% (67-100%). Of 9 pts with acute leukemia, 3 (33%) died from progressive disease. CD3, CD4, CD8, CD19 and CD56 counts at day +180/365 were normal in 20/38%, 0/13%, 40/63%, 70/100% and 100/100% of pts, respectively. Engraftment, GVHD, fungal infection and IR did not differ with respect to conditioning; MAC recipients had higher risk of viral infection ($p = .02$) and mortality (5/8 in MAC vs. 0/6 in RTC, but $p = .09$)

Conclusions: Rapid neutrophil engraftment, no PTLD, minimal grade II-IV aGVHD and high day 100 and overall survival were observed. Depletion of B and T cells during CD34 selection may be responsible for the relatively slow recovery of T cells post-transplant. These results support the continued investigation of CD34-selected MUD PBSCT in pediatric recipients.

Table 1. Stem cell selection data for patients undergoing CD34+-selected MUD PBSCT

	Median	Range
Pre-Selection $CD34^+$ x 10^6 total cells	438.79	239.75 - 886.41
Post-Selection $CD34^+$ x 10^6 total cells	299.57	131.81 - 521.94
$CD34^+$ Percent Recovery	58.88	42.93 - 85.58
Final Infused $CD34^+$ x 10^6/kg	5.06	2.02 - 13.30
Pre-Selection $CD3^+$ x 10^8/kg	4.74	2.30 - 20.69
Post-Selection $CD3^+$ x 10^5/kg	0.220	<0.001 - 2.450
$CD3^+$ Log Depletion	4.33	2.45 - *
$CD3^+$ Addback x 10^5/kg	1.003	0 - 2.170
Final Infused $CD3^+$ x 10^5/kg	1.500	0.093 - 2.600

*Post-selection $CD3^+$ was below the threshold of detection for two grafts.

242

ANALYSIS OF THE INCIDENCE AND CHARACTERISTICS OF VENOOCCLUSIVE DISEASE (VOD) OF THE LIVER IN PEDIATRIC HEMATOPOIETIC PROGENITOR CELL TRANSPLANT (HPCT) PATIENTS WITH HEPARIN ALONE VS. HEPARIN AND URSODIOL PROPHYLAXIS AT THE MEDICAL COLLEGE OF WISCONSIN

Talano, J.M.[1], Brown, J.[1], Casper, J.T.[1], Mulberry, M.[1], Eastwood, D.[2], Ahn, K.W.[2], Margolis, D.A.[1] [1]Medical College of Wisconsin, Milwaukee, WI; [2]Medical College of Wisconsin, Milwaukee, WI

VOD is a serious and potentially life-threatening complication of HPCT as a result of liver injury from the effect of chemotherapy and/or radiation. The reported incidence rate in pediatric HPCT patients varies widely from 5% to 40%. Previous studies have shown the beneficial effects of post-transplant pharmacological therapies such as ursodeoxyholic acid (ursodiol), heparin, and defibrotide at preventing VOD. However, the combined effect of heparin and ursodiol prophylaxis in preventing VOD in pediatric patients has yet to be determined. This study evaluated retrospectively whether there was a benefit of such combined therapy in pediatric HPCT patients. Our center adopted as standard practice for all HPCT patients the initiation of low dose heparin at 4 units/kg/hour with the commencement of conditioning for HPCT until day +28 post transplant. In 2003, we combined ursodiol 10 mg/kg TID to start with HPCT conditioning and to continue until day + 100 post transplant with low dose heparin through day + 28 for all pediatric HPCT patients.

We performed a retrospective chart review and compared the characteristics and the incidence of VOD in patients who underwent transplantation from 1996-2002 and received heparin alone compared to 2003-2008 when the patients received the combination of heparin and ursodiol prophylaxis. Patients were identified through medical records with the ICD diagnosis of VOD. The medical records were reviewed and those patients who did not meet the Baltimore criteria for the diagnosis of VOD were excluded. Only patients who developed VOD with their first transplants were included.

The 100 day incidence of VOD was 0.0605 (SE 0.01618) in group 1 and 0.0227 (SE 0.01002) in group 2. The difference is 0.0377 (SE 0.0190) and based on a standard normal distribution with a $p = 0.0473$. The day 100 survival in the VOD patients was 6 out of 13 in group 1 and 3 out of 5 in group 2. In conclusion, low dose heparin and ursodiol prophylaxis appears to be an effective strategy in VOD prevention in pediatric patients. The combination appeared to be more effective than heparin alone. However, this study is limited in that it is retrospective in nature. Future prospective trials need to be performed in pediatric HPCT patients to further elucidate the most efficacious and cost effective VOD prophylaxis, since currently there is no consensus of what constitutes standard of care among pediatric HPCT centers.

	Group 1 Heparin (216)	Group 2 Heparin + Ursodiol (220)
Allogeneic	187 (86.5%)	160 (72.7%)
Autologous	29 (13.5%)	60 (27.3%)
Median Age	9 yrs	8 yrs
Male	123 (57%)	135 (62%)
Non-malignant	34 (15.7%)	50 (22.8%)
Hematologic Malignancy	143 (66.2%)	109 (49.5%)
Non-hematologic Malignancy	39 (18.1%)	61 (27.7%)
# VOD	13	5

243

OUTCOMES OF MATCHED RELATED DONOR HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PEDIATRIC PATIENTS WITH MYELODYSPLASTIC SYNDROME

Parikh, S.H., Martin, P.L., Prasad, V.K., Szabolcs, P., Ciocci, G., Driscoll, T.A., Kurtzberg, J. Duke University Medical Center, Durham, NC

Myelodysplastic syndromes (MDS) in children are associated with significant morbidity and risk of leukemic transformation. Allogeneic hematopoietic stem cell transplantation is the only curative therapy. The ideal allogeneic donor is an HLA-identical sibling or